Induced pluripotent stem cell-derived hepatocytes have the functional and proliferative capabilities needed for liver regeneration in mice.

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Public Summary:
The study establishes that mouse induced pluripotent stem cells (iPSCs) generated in a clinically acceptable fashion can in principle give rise to hepatocytes that function and proliferate similar to primary hepatocytes. Recapitulating these results with hepatocytes derived from human iPSCs in cell culture is expected to provide the basis for an effective liver cell therapy.

Scientific Abstract:
The ability to generate induced pluripotent stem (iPS) cells from a patient's somatic cells has provided a foundation for organ regeneration without the need for immune suppression. However, it has not been established that the differentiated progeny of iPS cells can effectively reverse failure of a vital organ. Here, we examined whether iPS cell-derived hepatocytes have both the functional and proliferative capabilities needed for liver regeneration in mice with fumarylacetoacetate hydrolase deficiency. To avoid biases resulting from random genomic integration, we used iPS cells generated without viruses. To exclude compensation by hepatocytes not derived from iPS cells, we generated chimeric mice in which all hepatocytes were iPS cell derived. In vivo analyses showed that iPS cells were intrinsically able to differentiate into fully mature hepatocytes that provided full liver function. The iPS cell-derived hepatocytes also replicated the unique proliferative capabilities of normal hepatocytes and were able to regenerate the liver after transplantation and two-thirds partial hepatectomy. Thus, our results establish the feasibility of using iPS cells generated in a clinically acceptable fashion for rapid and stable liver regeneration.